#14

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: M. Rigdon Lentz

Serial No.: 09/699,003 Art Unit: 3762

Filed: October 26, 2000 Examiner: P. Bianco

For: *METHODS AND COMPOSITIONS FOR TREATMENT OF CANCERS*

Assistant Commissioner for Patents
Washington, D.C. 20231

APPEAL BRIEF

Sir:

This is an appeal from the office action mailed August 1, 2003, rejecting claims 1-5, 8, 12, 14 and 20. A notice of appeal was filed on December 1, 2003. Enclosed with this response is the appropriate fee for filing an appeal brief for a small entity. It is believed no further fees are due. However, if so, the Assistant Commissioner is authorized to charge any fees to our Deposit Order Account No. 50-1868.

Please note that a Supplemental Information Disclosure Statement was mailed on October 2, 2003. This has not been acted on.

No action has been received on the Amendment filed December 1, 2003.

(1) REAL PARTY IN INTEREST

The real party in interest of this application is the assignee, Biopheresis Technologies, LLC, Nashville, TN.

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(2) RELATED APPEALS AND INTERFERENCES

There are no pending related appeals or interferences known to appellant, the undersigned, or appellant's assignee which directly affects, which would be directly affected by, or which would have a bearing on the Board's decision in this appeal.

Appellant has requested an interference be declared with U.S. Patent No. 6,379,708 to Howell, et al. Appellant would be the senior party.

(3) STATUS OF CLAIMS ON APPEAL

Claims 1-7, 8-10, 12, and 16-20 are pending and on appeal. The text of each claim on appeal, as amended, is set forth in the Appendix to this Appeal Brief.

(4) STATUS OF AMENDMENTS

The claims were last amended in the amendment mailed January 24, 2003.

An amendment was filed December 1, 2003, but no action has been received. The only amendment was to correct a typographical error of the spelling of "immobilized".

(5) SUMMARY OF THE INVENTION

As summarized at page 2, line 26 to page 3, line 27, the claims are drawn to a method to treat cancer by selectively removing soluble receptor/inhibitors to soluble tissue necrosis factor receptor-1 ("sTNFR-1"), soluble tissue necrosis factor receptor-2 ("sTNFR-2"), soluble interleukin-2 receptor ("sIL-2R"), soluble interleukin-1 receptor ("sIL-1R"), soluble interleukin-6 receptor ("sIL-6R"), or soluble interferon-gamma receptor ("sIFN-gammaR") (claims 1-6 and 8-10) and system for use therein (claims 12 and 16-20). These can be removed by binding to the cytokine, an epitope thereof, or an antibody to the receptor (claims 9, 10, 18, and 19). These can be immobilized in the filter, in a column, or using other standard techniques for binding reactions to remove proteins from the blood or plasma of a patient (claim 19). The patient is preferably

treated daily for three weeks, diagnostic tests conducted to verify that there has been shrinkage of the tumors, then the treatment regime is repeated.

The treatment can be combined with an alternative therapy, for example, treatment with an anti-angiogenic compound, one or more cytokines such as TNF, gamma interferon, other interferons, or IL-2, or a procoagulant compound (claim 5). The treatment increases the inflammation against tumors by allowing cytokines, such as TNF, to work effectively. This provides a basis for an improved effect when combined with any treatment that enhances cytokine activity against the tumors, for example, treatments using alkylating agents, doxyrubicin, carboplatinum, cisplatinum, and taxol, and other drugs which may be synergistic in effect with "unblocked" cytokines. Alternatively, the ultrapheresis treatment can be combined with local chemotherapy, systemic chemotherapy, and/or radiation.

(6) ISSUES ON APPEAL

(a) Whether claims 1-5, 8, 12, 14 and 20 lack novelty under 35 U.S.C. 102(b) over U.S. Patent No. 4,708,713 to Lentz in combination with Selinsky, et al., Immunology 94(1):88-93 (1998).

(b) Whether claims 9, 10 and 16-19 are obvious under 35 U.S.C. 103 over '713 to Lentz in view of U.S. Patent No. 5,523,096 to Okamma, et al.; and

(c) Whether claim 6 is obvious under 35 U.S.C. 103 over Lentz and Selinsky in combination with U.S. Patent No. 5,861,483 to Wolpe

(7) GROUPING OF CLAIMS

The claims do not stand or fall together. Groupings and appropriate arguments are made below.

(8) ARGUMENTS

(a) The Claimed Invention

Appellant has discovered that it is possible to treat a disease such as cancer by selectively removing small molecular weight inhibitors that are produced by the cancerous cells to block the patient's immune system from killing the tumor.

The treatment is now in clinical trials in Europe, with extremely promising results, having produced remissions in a number of patients who had failed traditional chemotherapy and radiation treatments. Promising results have also been obtained in the treatment of patients with autoimmune disease such as multiple sclerosis.

It has long been believed that tumors must produce some type of blocking agent, that allowed the tumor(s) to grow, ultimately killing the patient. Traditional chemotherapy is based on the premise that one administers a cytotoxic agent that kills the more rapidly proliferating tumor cells at a higher rate than the normal cells. The disadvantages of this are immediately apparent – if the tumor cells are slow growing, chemotherapy is ineffective. If the cells become resistant, the chemotherapy is ineffective. In all cases, there is serious toxicity and other side effects.

Targeted chemotherapy was developed as an obvious corollary, targeting the toxic agent to a marker on the tumor cells but not on the normal cells. While this produced better results, it has been difficult to find a marker that could be targeted in all cases.

Many tumor markers are known. Two that are used as diagnostics, to indicate how much cancer is present, include prostate specific antigen ("PSA") and carcinoembryonic antigen ("CEA"). Studies to determine if one could target these antigens, or induce remission by removing them, failed.

Appellant arrived at his claimed method after many years. When he first started treating patients, he believe that the agent produced by the tumors was a large immunoglobulin complex, so he treated plasma to remove all high molecular weight molecules. This method is the subject of the Lentz '713 patent, discussed below. This induced remission, but required very expensive replacement of the albumin and left the patient's immunoglobulin at very low levels, thereby leaving him unprotected against infection.

Subsequent studies indicated that it was not an immunoglobulin complex protecting the tumors, and Dr. Lentz found that he could leave the immunoglobulin, allowing the patient to thereby retain better immunity. This was achieved by using a filter with a molecular weight cutoff of 120,000 daltons, instead of 150,000.

Further studies indicated that tumors produced low molecular weight molecules that were fragments of cytokine receptors, which were produced in large quantities in the blood, where they bound to the cytokines, preventing them from complexing with the tumor cells, leading to their death. Dr. Lentz then designed specific antibody columns, which selectively removed these inhibitors, inducing remission in tumor patients. The studies currently in progress remove three inhibitors: soluble tumor necrosis receptor 1, soluble tumor necrosis receptor 2, and a soluble cytokine receptor. The advantage of the selective removal is that the patient does not need either the albumin or immunoglobulin replaced, greatly lowering the cost of treatment, with the same or better efficacy.

(b) Rejections Under 35 U.S.C. § 102

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims. *Hybritech Inc v Monoclonal Antibodies Inc*, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 US 947

(1987); *Scripps Clinic & Research Found v Genentech Inc*, 18 USPQ2d 1001 (Fed. Cir. 1991). The Federal Circuit held in *Scripps*, 18 USPQ2d at 1010:

> Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . *There must be no difference* between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. (Emphasis added)

A reference that fails to disclose even one limitation will not be found to anticipate, even if the missing limitation could be discoverable through further experimentation. As the Federal Circuit held in *Scripps, Id.*:

> [A] finding of anticipation requires that all aspects of the claimed invention were already described in a single reference: a finding that is not supportable if it is necessary to prove facts beyond those disclosed in the reference in order to meet the claim limitations. The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill in the gaps in the reference.

For a prior art reference to anticipate a claim, it must enable a person skilled in the art to practice the invention. The Federal Circuit held that "a §102(b) reference must sufficiently describe the claimed invention to have placed the public in possession of it. . . [E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." *Paperless Accounting Inc v Bay Area Rapid Transit Sys.*, 231 USPQ 649, 653 (Fed. Cir. 1986) (citations omitted).

The examiner rejected claims 1-5, 8, 12, 14 and 20 as disclosed by a combination of two references, U.S. Patent No. 4,708,713 to Lentz, in combination with Selinsky, et al., Immunology 94:88-93 (1998).

It is believed this rejection is not appropriate under 35 U.S.C. 102(b), which requires a showing of all of the claimed elements in a single reference published more than one year before the effective filing date. By virtue of the examiner's reference to two different documents, clearly the rejection under 102(b) is inappropriate. The rejection would also be inappropriate under 35 102(b) as to Selinsky, which was published only weeks prior to Appellant's filing date.

In any event, neither reference discloses each of the claimed elements. Since it is believed the rejection was meant under 35 U.S.C. 103, the references are discussed in more detail below.

(c) Rejections Under 35 U.S.C. § 103

The law is quite clear that, for the Patent Office to establish a *prima facie* case of obviousness of claimed subject matter, the prior art references relied upon must provide *both* a suggestion to make the claimed invention and a reasonable expectation of success. It is also clear that the whole field of the invention must be considered, including those publications which teach away from the claimed invention. Particularly relevant to the matters under consideration here are the decisions of the Court of Appeals for the Federal Circuit in *In re Dow Chemical*, 5 USPQ2d 1529 (1988) and *In re Vaeck*, 20 USPQ2d 1438 (1991). The *Dow* Court noted that:

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in light

> of the prior art.... Both the suggestion and expectation of success must be founded in the prior art, not in the applicant's disclosure.
>
> In determining whether such a suggestion can fairly be gleaned from the prior art, *the full field of the invention must be considered*: for the person of ordinary skill is charged with knowledge of the entire body of technological literature, including that which might lead away from the claimed invention.... Evidence that supports, rather than negates, patentability must be fairly considered.

5 USPQ 2d at 1531-1532 (Citations omitted, emphasis added).

In *In re Dow Chemical*, a combination of three components forming an impact resistant rubber-based resin was not found to be obvious based upon art disclosing the individual components. The court noted that the record had shown that the claimed combination had previously been made, *but did not produce the product desired.* "That there were other attempts, and various combinations and procedures tried in the past, does not render obvious the later successful one.... Recognition of need, and difficulties encountered by those skilled in the field, are classical indicia of unobviousness," *Id.* at 1531 (citations omitted). The Court found that none of the prior art cited by the Appellant and the PTO suggested that any process could be used successfully in this three-component system to produce the product having the desired properties. Further, the Court stated that evidence from an expert expressing skepticism as to the success of the claimed combination before these inventors proved him wrong should be considered. *Id.* at 1532.

The prior art must provide one of ordinary skill in the art with the motivation to make the proposed modifications needed to arrive at the claimed invention. *In re Geiger*, 815 F.2d 686, 2 U.S.P.Q.2d 1276 (Fed. Cir. 1987); *In re Lalu and Foulletier*, 747 F.2d 703, 705, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984). Claims for an invention are not *prima facie* obvious if the primary references do not suggest all elements of the claimed invention and the prior art does not suggest the modifications that would bring the primary references into conformity with the application claims. *In re Fritch*, 23 U.S.P.Q.2d, 1780 (Fed. Cir. 1992). *In re Laskowski*, 871 F.2d 115 (Fed. Cir. 1989). This is not possible when the claimed invention achieves more than what any or all of the prior art references allegedly suggest, expressly or by reasonable implication.

Lentz

Lentz describes removal of a large number of proteins using a filter. The only selectivity is by virtue of the molecular weight cutoff of the filter, which is approximately 200,000. ALL proteins in the plasma with the possible exception of some IgM will pass through a filter with a cutoff of 200,000. Therefore the limitations of claims 1-5, 8, 12 and 20 are not met.

Assuming the examiner meant to make a rejection under 35 U.S.C. 103, Selinsky does not make up for the deficiency of Lentz. Lentz teaches away from the selective removal of soluble cytokine receptor molecules. See col. 6, lines 34 to 46, of Lentz, which states that there are two inhibitors being removed, one, an IgG immunoglobulin type molecule (lines 39-44) and the other which is believed to be a high molecular weight compound (mw between 200,000 and 1,000,000). Neither could possibly be construed to be a soluble cytokine inhibitor such as soluble TNF receptor, which has a significantly lower molecular weight. Moreover, Lentz clearly does not know what the inhibitor(s) are, indicating that there are multiple inhibitors. In summary, Lentz teaches one of ordinary skill in the art that (1) the inhibitors are high molecular

weight proteins and (2) there are more than one inhibitors involved in immunosuppression of the anti-tumor response, neither of which is a cytokine type molecule.

Selinsky

Selinksky describes an experiment to correlate the levels of soluble tissue necrosis factor receptor ("sTNFR") with tumor burden. This in no way makes obvious the removal of sTNFR to treat tumors or other disorders. The standard under 35 U.S.C. 103 is whether the prior art leads one of ordinary skill in the art to combine the prior art as applicant has done, ***with a reasonable expectation of success.***

The prior art at the time this application was filed in May 1998, was that there were a number of tumor markers that correlated with tumor burden. The most well known include the prostate specific antigen ("PSA") and carcinoembryonic antigen ("CEA"). Studies had been conducted to remove both PSA and CEA, with the hope of decreasing tumor burden. Neither had been effective. Therefore, one skilled in the art would have had no expectation of success that removal of a soluble cytokine receptor such as sTNFR would be effective.

Indeed, this is clearly the opinion shared by the authors of the paper. The Declaration under 37 C.F.R. 1.132 filed in U.S.S.N. 09/444,144, which subsequently issued as U.S. Patent No. 6,379,708 to Howell, et al., distinguished the same art, one of which was their own. Please see pages 2-3 of the declaration, discussing first the Lentz patent and then the Selinksky paper. As the authors of the Selinsky paper noted:

> "It is submitted that, although the statement in Selinsky et al. may cause one of skill in the art to consider how to antagonize or remove sTNFR1 *in situ*, such a statement is merely an invitation to experimentation and opens the door for one of skill in the art to consider a wide range of possible approaches. Indeed,

Selinsky et al. provides absolutely no guidance as to how one of skill in the art would go about such a task, but rather generally state that the "therapeutic utility of manipulating sTNFRI levels *in vitro* has been demonstrated" and that "sTNFRI effectively inhibits immune responses *in vivo* and ...its modulation is a legitimate therapeutica avenue."

It is submitted that one of skill in the art, when presented with an invitation to manipulate the effects of a soluble protein, would look to a variety of conventional approaches to remove or manipulate the effects of that soluble protein *in vivo*, because such approaches are the most clinically desirable means of treating a patient."

For the same reasons that the examiner allowed the claims in the Howell patent over the combination of Lentz and Selinsky, so are the claims in this application allowable over Lentz and Selinsky.

Lentz and Selinsky are discussed above. Neither Okarma nor Wolpe make up for the deficiencies of Lentz and Selinsky. Okarma does no more than describe immunoaffinity columns for removal of cytokines for treatment of disorders such as septic shock. Wolpe describes the role of some cytokines in mounting an immune response. Wolpe teaches away from what is claimd by suggesting one should administer cytokines, not put in soluble receptor molecules.

The prior art fails to teach one of ordinary skill in the art, with a reasonable expectation of success, that one should remove soluble cytokine receptors, my any means, much less an immunoabsorbent column, to treat a disease such as cancer. Lentz teaches that if one removes every protein in the plasma having a molecular weight of about 48,000 (albumin) or larger,

tumor reduction will occur. The test under 103 is whether one skilled in the art would be led, by the reference, to combine the references, as applicant has done, with a reasonable expectation of success. There is simply nothing in these references that leads one to that conclusion. The result is simply too unpredictable. Applicant has now conducted numerous trials in humans with a variety of different cancers, and shown that selective removal of soluble cytokines such as sTNFR1 and sTNFR2 does result in an inflammatory response resulting in substantial decrease in tumor volume. This is enhanced by treatment with other types of therapy, including chemotherapy, hyperthermia, and radiation.

The prior art, in combination, says that one should remove ***many proteins, including soluble cytokines*** (which are of a lower molecular weight than albumin) if one wants to treat tumors. Selinsky is merely an invitation to experiment, a discussion of an interesting observation – not a showing that sTNFR could be removed and cause tumor reduction. The prior art provides numerous examples of other tumor burden markers whose removal does not correlate with tumor reduction. The results obtained by applicant are simply too unpredictable.

(d) **The Examiner has failed to examine the dependent claims separately**

Claim 5 requires treating the tissue with an agent selected from the group consisting of anti-angiogenic compounds, procoagulant compounds, cytokines, chemotherapeutic agents, and radiation. None of the art cited by the examiner provides any teaching that would lead one to treat patients, particularly patients who have already failed treatment with chemotherapeutic agents, to be treated again with these agents. However, appellant's studies have demonstrated that these additional agents, following or administered with the selective removal of the inhibitors, does impart additional benefit.

Claim 6 defines the cytokine as GM-CSF, erythropoietin, thrombopoetin, G-CSF, M-CSF and SCF. None of the prior art teaches that one should remove soluble inhibitors of these molecules. Indeed, none of the art even mentions inhibitors of these cytokines.

None of the art teaches removing a cytokine receptor using an antibody column, as required by claims 8, 9, 10, 12, and 16-19. Selinsky only measures the presence of soluble tumor necrosis factor in cell culture. Lentz only discloses filtration.

(e) **There is a later filed patent claiming the same subject matter**

As noted above, U.S. Patent No. 6,379,708 to Howell, which is an issued U.S. patent, discloses and claims common subject matter. Howell was issued only after filing of a declaration under 37 C.F.R. 1.131 (one which the undersigned believes was clearly defective). Applicant requests declaration of an interference to resolve the issue of who is entitled to a patent. Howell's earliest priority date is November 20, 1999. This application claims priority as a continuation of U.S.S.N. 09/316,226 filed May 21, 1999, which is a continuation in part of U.S.S.N. 09/083,307 filed May 22, 1998. Accordingly, Lentz should be declared the senior party.

A proposed count is as follows:

A method of stimulating an immune response in a mammal having a pathological condition comprising:

Contacting the acellular component of blood from a mammal with a binding partner capable of specifically binding to a targeted immune system inhibitor selected from the group consisting of soluble receptors for tumor necrosis factor, interleukin-1 receptor antagonist, soluble receptor for interferon-gamma, soluble receptors for interleukin-1 and soluble receptors for interleukin-6,

Removing the binding partner bound to the targeted immune system inhibitor from the acellular component to produce an altered acellular component having a reduced amount of the targeted immune system inhibitor, and

Administering the altered acellular component, or blood combined with altered acellular component, to the mammal.

This count corresponds to all claims of Howell. Claims 37-44 are further restricted to where the means for binding the targeted immune system inhibitor is an antibody bound to an inert medium to form an absorbent matrix.

This count corresponds to claims 1-4 and 8-10 of the present application.

(9) SUMMARY

The prior art fails to disclose in a single reference each element of the claims. Accordingly, the claims should not be rejected under 35 U.S.C. 102.

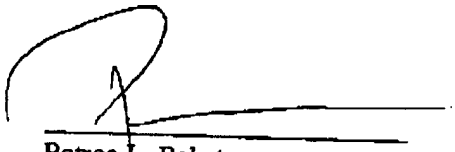
The prior art fails to disclosure either the claimed elements, the motivation to combine as appellant has combined, or anything that would lead one of skill in the art to have a reasonable expectation of success in doing so. Accordingly, the claims should not be rejected under 35 U.S.C. 103.

A patent has issued on a much later filed patent application, claiming the same subject matter, and allowed over the same prior art. The claims in this application should also be allowed, and an interference declared, so that priority of invention can be established.

(10) CONCLUSION

For the foregoing reasons, claims 1-6, 8-10, 12 and 16-20 should be allowed and an interference declared.

Respectfully submitted,



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APPENDIX: Claims on Appeal

1. (previously once amended) A method for inducing an immune response against transformed, infected or diseased tissue comprising

selectively removing soluble cytokine receptor molecules until the transformed, infected, or diseased tissue is reduced in amount.

2. (original) The method of claim 1 wherein the tissue is a solid tumor.

3. (original) The method of claim 1 wherein the components are removed from one blood volume.

4. (original) The method of claim 1 wherein the components are removed in multiple treatments.

5. (original) The method of claim 1 further comprising treating the tissue with an agent selected from the group consisting of anti-angiogenic compounds, procoagulant compounds, cytokines, chemotherapeutic agents, and radiation.

6. (original) The method of claim 5 whercin the agent is a cytokine and the cytokine is selected from the group consisting of GM-CSF, erythropoietin, thrombopoetin, G-CSF, M-CSF and SCF.

Claim 7 cancelled.

8. (previously once amended) The method of claim 1 wherein the soluble cytokine receptor molecules are selected from the group consisting of soluble tissue necrosis factor receptor-1 ("sTNFR-1"), soluble tissue necrosis factor receptor-2 ("sTNFR-2"), soluble interleukin-2 receptor ("sIL-2R"), soluble interleukin-1 receptor ("sIL-1R"), soluble interleukin-6 receptor ("sIL-6R"), and soluble interferon-gamma receptor ("sIFN-gammaR").

9. (original) The method of claim 8 wherein the cytokine receptor molecules are removed by binding to the cytokine or to an antibody or antibody fragment immunoreactive with the cytokine receptor molecules.

10. (previously presented) The method of claim 9 wherein the cytokine or antibody or antibody fragments are immobilized in a filter or column through which the patient's blood or plasma is circulated prior to being returned to the patient.

Claim 11 cancelled.

12. (previously once amended) A system for inducing an immune response against transformed, infected or diseased tissue comprising

a device for selectively removing soluble cytokine receptor molecules, having inlet and outlet means for connection to a pump and tubing to recirculate the blood of a patient through the device.

Claims 13-15 cancelled.

16. (original) The system of claim 12 wherein the device is an absorbant colum selectively removing specific cytokine or cellular inhibitors from the blood.

17. (original) The system of claim 16 wherein the cytokine or cellular inhibitors are selected from the group consisting of soluble tissue necrosis factor receptor-1 ("sTNFR-1"), soluble tissue necrosis factor receptor-2 ("sTNFR-2"), soluble interleukin-2 receptor ("sIL-2R"), soluble interleukin-1 receptor ("sIL-1R"), soluble interleukin-6 receptor ("sIL-6R"), and soluble interferon-gamma receptor ("sIFN-gammaR").

18. (original) The system of claim 17 comprising cytokines or antibody or antibody fragments immunoreactive with the cytokine receptor molecules.

19. (original) The system of claim 18 wherein the cytokine or antibody or antibody fragments are immobilized in a filter or column through which the patient's blood or plasma is circulated prior to being returned to the patient.

20. (original) The system of claim 12 wherein the blood is plasma.

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PTO/SB/17 (10-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☑ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 165.00

Complete if Known	
Application Number	09/699,003
Filing Date	October 26, 2000
First Named Inventor	M. Rigdon Lentz
Examiner Name	P. Biano
Art Unit	3762
Attorney Docket No.	LEN 101 CIP CON

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☑ Deposit Account:

Deposit Account Number: 50-1868

Deposit Account Name: Holland & Knight LLP

The Director is authorized to: *(check all that apply)*

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☑ Charge any additional fee(s) or any underpayment of fee(s)

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims		Fee from below	Fee Paid
Total Claims	-20** =		x	=
Independent Claims	-3*** =		x	=
Multiple Dependent				=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	*** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	165.00
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid SUBTOTAL (3) ($) 165.00

SUBMITTED BY

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Signature				Date	February 2, 2004

(Complete *(if applicable)*)

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Applicants:	M. Rigdon Lentz		
Serial No.:	09/699,003	Art Unit:	3762
Filed:	October 26, 2000	Examiner:	P. Bianco
For:	*METHODS AND COMPOSITIONS FOR TREATMENT OF CANCERS*		

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Filing Date	October 26, 2000
First Named Inventor	M. Rigdon Lentz
Art Unit	3762
Examiner Name	P. Bianco
Attorney Docket Number	LEN 101 CIP CON

ENCLOSURES (Check all that apply)

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